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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE



In re the Application of)	Group Art Unit: 1631
Michael Grunstein et al.)	Examiner: J. Lundgren
Serial No: 09/261,104)	
Filed: March 3, 1999)	Response to Paper No. 9
For: COMPOSITIONS AND METHODS)	
FOR THE TREATMENT OF)	
ASTHMA)	

SUPPLEMENTAL RESPONSE UNDER 37 C.F.R. §1.111

As indicated in the response filed February 28, 2001 to the outstanding Official Action dated August 30, 2001, in the above identified application, Applicants hereby submit a Declaration under 37 C.F.R. §1.131 showing evidence of conception and diligent reduction to practice of the claimed invention. It is believed that this Declaration provides evidence to overcome the §102(e) rejection based upon US Patent 6,011,138 to Reff et al. Accordingly, Applicants again request that the rejection of claims 1-4 based on Reff et al. be withdrawn.

Favorable consideration leading to prompt allowance of the present application is respectfully requested.

Respectfully submitted,
DANN, DORFMAN, HERRELL AND SKILLMAN
A Professional Corporation

By Kathleen D. Rigaut
Kathleen D. Rigaut, Ph.D., J.D.
PTO Registration No. 43,047

Telephone: (215) 563-4100

In the event that a fee is required in connection with this submission and not enclosed, the Commissioner is authorized to charge such fee to the account if the undersigned attorneys, Account No. 04-1406. A duplicate copy of this sheet is enclosed.

Kathleen D. Rigaut
Kathleen D. Rigaut, Ph.D., J.D.

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DECLARATION OF MICHAEL GRUNSTEIN AND HAKON HAKONARSON

We, Michael Grunstein and Hakon Hakonarson, hereby declare that:

1. We are the inventors of the invention described and claimed in U.S. Patent Application Serial No. 09/261,104 (the '104 application).

2. We have read and are familiar with the contents of the official Action dated August 30, 2000 in the '104 application. We note that the Examiner has rejected claims 1-4 under 35 U.S.C. §102(e) as allegedly anticipated by US Patent 6,011,138 to Reff et al. (hereinafter the '138 application). The purpose of this declaration is to establish that the invention described and claimed in the '104 application (the "subject invention") was conceived of prior to the February 20, 1997, which upon information and belief, is the earliest effective filing date of the '138 application and diligently and constructively reduced to practice at least as early as March 3, 1998, the filing date of the provisional application from which the instant application claims priority under 35 U.S.C. §119(e).

3. Conception of the invention described in the present application is evidenced by a copy of an abstract (Exhibit A)

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and copies of notebook pages submitted herewith as Exhibit B1-B7. The dates on the data have been masked for the purpose of this Declaration. Described in the notebook pages are experiments utilized in the development of methods for the treatment of asthma. The present inventors observed that airway smooth muscle tissue (ASM) treated with atopic asthmatic serum demonstrates increased constrictor and reduced relaxation response to acetylcholine and isoproterenol when compared to control serum-treated tissue. These results are described in Exhibit A which is an abstract submitted to ALA/ATS International Conference prior to the earliest effective filing date of the '138 patent. The data in Exhibits B1-B7 reveal that the effects of atopic asthmatic serum are blocked or prevented by preincubation of ASM with an anti-CD23 monoclonal antibody. B1 is a graph of the tracing data presented in Exhibits B6 and B7. The experiments presented in Exhibits B1-B7 were also performed prior to February 20, 1997. Conception of the subject matter described in Exhibits A and B occurred in the United States.

4. Attached hereto as Exhibits C1 and C2 are pages from our laboratory notebooks describing Southern blots showing that the FcεRII receptor (CD23) is expressed in airway smooth muscle cells and that this expression is upregulated by exposing the cells to atopic asthmatic serum. These results were observed in both human (C1) and rabbit (C2) tissue. We performed these experiments and contemporaneously recorded the data set forth in the laboratory notebook pages of Exhibit C. The dates appearing in Exhibit C have been masked for the purpose of this Declaration.

5. The results of flow cytometry analysis of CD23 expression are shown in Exhibits D1-D3. Airway smooth muscle tissue was exposed to atopic asthmatic serum for 24 hours. The data show that relative to isotype negative control

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antibody (D1) CD23 expression was dramatically upregulated in human asthmatic serum-treated human airway cells (D2) relative to control serum-treated cells (D3).

6. Exhibit E shows the results of experiments performed using airway smooth muscle tissue obtained from human patients. Representative Southern blots are shown revealing that, in contrast to lung tissue, a dramatic increase in CD23 expression is seen in airway smooth muscle tissue of asthmatic patients relative to control non-asthmatic patient tissue.

7. In order to show a reduction to practice of our invention, Exhibit F is attached hereto. Exhibit F is a copy of the provisional application filed March 10, 1998 from which the instant application claims priority under 35 U.S.C. §119(e).

8. After conceiving the invention and carrying out the experimentation described in paragraphs 3-6 above, we were diligent in reducing the invention to practice, including the period from just prior to February 20, 1997 until the invention was subsequently reduced to practice as set forth in paragraph 7 above. The Exhibits described in paragraphs 3-6 describe our work during the relevant period. Thus, we conceived of the present invention prior to the filing date of the '138 application and thereafter diligently reduced the claimed invention to practice.

9. All of the experiments, the results of which are presented in the Exhibits attached to this Declaration, were performed by us or under our direction and supervision.

We hereby declare that all statements made herein of our own knowledge are true and that all statements made on information and belief are believed true; and further

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that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful statements may jeopardize the validity of the above-referenced application or any patent issued thereon.

April 19, 2001
DATE

April 19, 2001
DATE

Michael M. Grunstein
Michael M. Grunstein, M.D., Ph.D.
Hakon Hakonarson
Hakon Hakonarson, Ph.D.